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10/586,688	11/06/2006	Makoto Suematsu	K2100.0001	7334

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DICKSTEIN SHAPIRO LLP
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NEW YORK, NY 10019

EXAMINER

NOBLE, MARCIA STEPHENS

ART UNIT	PAPER NUMBER
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1632

MAIL DATE	DELIVERY MODE
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02/19/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/586,688	Applicant(s) SUEMATSU ET AL.	
	Examiner MARCIA S. NOBLE	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 and 12-21 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 12-21 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 July 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Withdrawn Rejections

The rejection of claims 1-10 and 12-21, under 35 U.S.C. 102(b) as being anticipated by Kazuo et al (JP 07-089874 (publication date: 4/04/1995; abstract is of record in the IDS, filed 7/20/2006; translation p. 1-23 provided by STIC translation), as evidenced by Dictionary.com (<http://dictionary.reference.com/browse/tinge>), is withdrawn. Applicant amended the claims to recite that the claimed carrier comprises DPEA. Kazuo does not disclose this limitation.

The rejection of claims 1-10 and 12-16, under 35 U.S.C. 102(e) as being anticipated by Tsuchida (US 6,949,663 B2 date:9/27/2005; effective filing date:11/9/2001), is withdrawn. Applicant amended the claims to recite that the claimed carrier comprises DPEA. Tsuchida does not disclose this limitation.

The rejection of claims 1-10 and 12-21 are, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn. Applicant removed the indefinite limitation of "a carboxylic type lipid".

The rejection of claims 1-10, on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,949,663, is withdrawn. Applicant amended the claims to more narrowly recite that the claimed carrier comprises DPEA. US 6,949,663 and the claims of this patent does not disclose or contemplate this limitation.

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The rejection of claim 17 under 35 U.S.C. 112, first paragraph because the specification does not enable the claim, is withdrawn. Applicant amended the claims to recite, "damaged endothelial cell site of tissue", which obviates the issue of enablement for claim 17.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-21, as amended or previously presented, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A drug delivery method comprising administering the pharmaceutical composition of claim 12 to a damaged endothelial cell site of tissue comprising endothelial cells in a subject, and allowing said composition to accumulate on the damaged endothelial cell site, and;

A drug control method comprising administering the pharmaceutical composition of claims 12 to a damaged endothelial cell site of tissue comprising endothelial cells in a subject, allowing said composition to accumulate on the damaged endothelial cell site, and allowing the drug to act on the damaged site.

The specification does not reasonably provide enablement for a method that does not administer the carrier specifically to a site of endothelial cell tissue damage.

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The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make or use the claimed invention, if not, whether an artisan would require undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is “undue”.

The method of claim 18 encompasses a drug delivery method that does not have the active step of administering the carrier comprising a drug to a subject. It is well established in the art for a drug to be delivered to a site of tissue damage it must be administered to a site of tissue damage. The teachings of the specification clearly teach that the instant invention is meant to treat sites of tissue damage and individuals (p. 1, line 12 to p. 2, line 21). However, the claims do not require administering the carrier. Therefore, for the claimed method to be enabled by the specification, the instant claims required an active administration step because the invention would not function without such an administration step.

Overall, the instant claims embrace carriers and methods of using such carrier in a way that is not enabled by the specification. The specification clearly teaches that the carrier functions by accumulation on endothelial cells. However, the breadth of the claims also encompasses a drug delivery method that does not administer the drug carrier. From the specification and teachings well established in the art, clearly these embodiments would not function. Therefore, these embodiments are not enabled by the specification. Therefore the instant claims are only enabled for the embodiments disclosed above.

Response to Arguments

Applicant's arguments filed 11/12/2009 have been fully considered but they are not persuasive. Applicant asserts that amending the claims to recite "damaged endothelial cell site" obviates the enablement rejection of record. Applicant's arguments are not found persuasive because while this amendment does address some of the enablement issues of record, other enablement issues remain for claims 18-21, as discussed above.

The following rejections are necessitated by the amendments to the claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-10 and 12-21 rejected under 35 U.S.C. 103(a) as being unpatentable over Kazuo et al (JP 07-089874 (publication date: 4/04/1995; abstract is of record in the IDS, filed 7/20/2006; translation p. 1-23 provided by STIC translation), as evidenced by Dictionary.com (<http://dictionary.reference.com/browse/tinge>).

Kazuo et al teaches a drug carrier tinged with positive charges in its surface that recognizes a blood vessel endothelium damage (p. 4, [0013], lines 1 to p. 5, line 2). According the Dictionary.com., the definition of "tinge" is "a slight admixture, as of some qualifying property or characteristic; trace; smattering" (see page 1 of Dictionary.com printout, definition # 4). Kazuo et al teaches a drug carrier with only trace amount of positive charge on its surface which would not affect the overall neutral or anion charge. Therefore, Kazuo et al teaches a non-cationic surface drug carrier as claimed, as evidenced by Dictionary.com. Furthermore, Kazuo et al teaches that the carrier can be made with such phospholipids as phosphatidylcholine, phosphatidylglycerol, and phosphatidylethanolamine (p. 6, [0036], line 1 to p. 7, line 3). These are the same material disclosed by specification for the production of the claimed carrier (See page 9, lines 5-22). Kazuo et al teaches that the carrier also comprises stabilizing agents such as sterols and palmitic acids (p. 7, [0037], line 1 and [0041], lines 1-3). Because Kazuo et al and the specification disclose carrier that are made of the same structural components, inherently the carriers of the instant claims and the carrier taught by Kazuo et al are the same. Also because the instantly claimed carrier and the carrier taught by

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Kazuo et al are the same, the carrier taught by Kazuo et al inherently has all the same functional properties and can be used for all the disclosed used in claims 1-10.

“Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972)).” “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” See also MPEP 2113.

In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01.

Katzuo et al teaches the drug carrier that can be used anti-inflammatory agents, anticancer agents, angiotensin conversion enzyme inhibitor, agents that inhibit smooth muscle cell mobilization, platelet aggregating repressors, and overall inhibitors of thrombolysis (p. 5, [0025], lines 1-6). Therefore, Katzuo et al teaches the limitations of drug transporter and pharmaceutical composition of claims 11-16.

Katzuo et al teaches that the liposome of their invention is administered intravenously to rats comprising blood vessel damage and liposome accumulation was monitored (p. 13, [0091], line 1 to [0092], line 6). Katzuo et al teaches that the liposome accumulated in the endothelial site of blood vessel damage (p. 13, [0096], line 4 to p. 14, line 1). Katzuo teaches the use of the liposome to deliver drugs that depress blood vessel thickening in a site of endothelial cell damage (p. 15, [0113], lines 1-4). Katzuo teaches that the liposome successfully delivered said drugs and blood vessel thickening was suppressed at the site of damage (p. 16, [0116], lines 1-2). Therefore, Katzuo et al teaches a method comprising accumulation of the carrier at a damage site in a blood vessel and allowing the drug to act on the damaged site, as claimed in claims 17-21.

Katzuo et al does not teach the use of specific palmitic acid equivalent, 1,5-dipalmitoyl-L-glutamate-succinic acid (DPEA). DPEA is a known species of palmitic acid in the prior art.

The combination of prior art cited above in all rejections under 35 U.S.C. 103 satisfies the factual inquiries as set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Once this has been accomplished the holdings in KSR can be applied (*KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. 389, 82 USPQ2d 1385

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(2007): "Exemplary rationales that may support a conclusion of obviousness include: (A) Combining prior art elements according to known methods to yield predictable results; (B) Simple substitution of one known element for another to obtain predictable results; (C) Use of known technique to improve similar devices (methods, or products) in the same way; (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results; (E) "Obvious to try" - choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention."

In the present situation, rationale E is applicable. It would have been obvious to an artisan of ordinary skill at the time the invention was made to choose from a finite number of predictable species of palmitic acid equivalents with a reasonable expectation of successfully producing a functional carrier as claimed. Thus, the teachings of the cited prior art in the obviousness rejection above provide the requisite teachings and motivations with a clear, reasonable expectation. The cited prior art meets the criteria set forth in both Graham and KSR.

Claims 1-10 and 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuchida (US 6,949,663 B2 date:9/27/2005; effective filing date:11/9/2001).

The applied reference has a common inventor (Shinji Takeoka) with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Tsuchida a carrier comprising the structural elements of a carboxylic type lipid that has no phosphate group (col 1, lines 58-59). The preamble of the claim also indicates that carrier has a non-cationic surface. Tsuchida teaches that the carboxylic lipid is stably fixed to phospholipid bilayer membranes (col 1, lines 60-63). Tsuchida teaches that linear hydrocarbon group can be introduced using a palmitic acid (col 5, line 60 to col 6, line 13). Tsuchida teaches that cholesterol, which is a type of sterol, is commonly used in the membranes (col 1, lines 29-30). Claim 1 also recites, "which can accumulate on a damaged endothelial cell site of a tissue comprising endothelial cells". These limitations do not add additional structural limitations to the claims carrier. Therefore, these teachings by Tsuchida encompass the limitations of claims 1 and 2 and inherently, the disclosed carrier should "accumulate on a damaged endothelial cell

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site of a tissue comprising endothelial cells” because the structure of Tsuchida is the same as claimed carrier.

Claims 3-10 also do not provide any additionally structural limitations. Therefore, the teachings by Tsuchida encompasses the limitations of claims 3-10.

Claim 12 encompasses pharmaceutical composition of claim 1 incorporating or carrying a drug. Given its broadest reasonable interpretation, “incorporating or carrying a drug” encompasses the presence of any substance in the carrier carried by or that is part of the carrier that is deliverable to a subject. Therefore, the carrier itself can be considered a drug and encompasses the limitations of the claims. Tsuchida teaches that the carboxylic lipids incorporated into membrane vesicles are administered to the body and used in pharmaceutical compositions (col 1, lines 20-24, col 2, lines 60-65, and col 13, lines 64-67). Claim 13 recites that the carrier functions as a drug for controlling a platelet function. Tsuchida teaches that the carboxylic lipid composition prevents aggregation of platelets (col 1, lines 60-67), therefore disclosing a drug for controlling a platelet function. Claim 14 specifies that the drug is a substance that is activated by inflammatory cells and is an antithrombotic agent. Tsuchida teaches that the liposome components cause thrombocytopenia and dysfunction of white blood cells (col 1, lines 36-39) and the carboxylic lipid counter these side effects (col 1, lines 48-53). Therefore, Tsuchida teaches the limitations of claims 14-16.

“Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently

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possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972)). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." See also MPEP 2113.

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Tsuchida does not teach the use of specific palmitic acid equivalent, 1,5-dipalmitoyl-L-glutamate-succinic acid (DPEA). DPEA is a known species of palmitic acid in the prior art.

The combination of prior art cited above in all rejections under 35 U.S.C. 103 satisfies the factual inquiries as set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Once this has been accomplished the holdings in KSR can be

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applied (*KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. 389, 82 USPQ2d 1385 (2007): "Exemplary rationales that may support a conclusion of obviousness include: (A) Combining prior art elements according to known methods to yield predictable results; (B) Simple substitution of one known element for another to obtain predictable results; (C) Use of known technique to improve similar devices (methods, or products) in the same way; (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results; (E) "Obvious to try" - choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention."

In the present situation, rationale E is applicable. It would have been obvious to an artisan of ordinary skill at the time the invention was made to choose from a finite number of predictable species of palmitic acid equivalents with a reasonable expectation of successfully producing a functional carrier as claimed. Thus, the teachings of the cited prior art in the obviousness rejection above provide the requisite teachings and motivations with a clear, reasonable expectation. The cited prior art meets the criteria set forth in both *Graham* and *KSR*.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **MARCIA S. NOBLE** whose telephone number is (571)272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Thaia N. Ton/
Primary Examiner, Art Unit 1632